Original Article

MEDICINE PALLIATIVE CARE

DOI: 10.47582/jompac.1221710

J Med Palliat Care 2023; 4(1): 69-73

The incidence and risk factors of thrombosis due to central venous catheter in SARS-CoV-2 patients in intensive care

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Cite this article as: Kahraman A, Eraslan Doğanay G. The incidence and risk factors of thrombosis due to central venous catheter in SARS-CoV-2 patients in intensive care. J Med Palliat Care 2023; 4(1): 69-73.

ABSTRACT

Aim: SARS-CoV-2 can cause an increase in both arterial and venous thrombotic events. It is thought that thrombotic events increase in patients due to deep hypoxia, which is the most serious symptom of patients, and the associated immobility.

Material and Method: 233 patients who were followed up in the 3rd Level COVID Intensive Care Unit of the hospital between 2021-2022 were retrospectively analyzed. It was determined that central venous catheter was applied to 110 patients. The age, gender, BMI, co-morbidities of the patients, and which central venous route is preferred for the catheter will be determined. In addition, the number of punctures, thrombocyte count as well as the use of anticoagulants and acetylsalicylic acid, whether or not he/she received total parenteral nutrition (TPN), and how many days the catheter was left will be recorded and thrombotic events will be determined.

Results: COVID-19 causes vascular pathologies as well as respiratory symptoms. Central venous catheter application is frequent in intensive care due to both treatment and nutritional support, and venous path preference affects the risk of thrombosis. Performing more than one catheter application from the same area, catheter duration and position of the end part of the catheter are important factors for the development of thrombosis. It has been found that thrombotic events related to femoral catheter have increased in SARS-CoV-2 patients hospitalized in intensive care. In our study, although the duration of femoral catheter use was low, the thrombosis rate was found to be high, which supports the literature. This situation has led us to reduce femoral catheter applications in intensive care SARS-CoV-2 patients hospitalized in our clinic and to prefer other catheterization methods.

Conclusion: In this study, the incidence of thrombosis was found to be higher in patients treated in the intensive care unit due to SARS-CoV-2 infection and who underwent femoral central catheterization compared to the literature.

Keywords: COVID -19, femoral vein, intensive care, SARS-COV-2, thrombosis

INTRODUCTION

SARS-CoV-2 disease commonly causes intravascular thrombosis, causing serious morbidity and mortality. The fact that patients are mostly immobile in intensive care and the increase in immobility due to desaturation by movement may also cause an increase in thrombotic events. A clear mechanism related to thrombotic events has not been proven and many theories can be proposed (1). SARS-CoV-2 accesses host cells through the angiotensin converting enzyme 2 protein, which is abundant in the lungs. This, in turn, affects the endothelial cells and leads to vascular lesions as a result of significant inflammatory syndrome and coagulation. SARS-CoV-2 virus uses angiotensin-converting enzyme 2 (ACE-2) receptors located in the endothelial layer of the respiratory tract, intestines, heart and vessels as an entry gate into the cell (2). Literature data indicate that the mediator of the serious and critical condition developing in COVID-19 patients is the state of hypercoagulation, which is characterized by micro- and macro vascular thrombotic angiopathy (3,4). It has been mentioned in research that hypercoagulation may be a consequence of viral infection caused by overexpression of ACE-2, which is used by SARS-CoV-2 as a receptor for entry into the cell in endothelial cells (3,4). In this study, we aimed to investigate peripheral vascular pathologies, the incidence of thrombosis due to central venous catheter and risk factors in SARS-CoV-2 patients in intensive care.

MATERIAL AND METHOD

The study was carried out with the permission of Ankara Atatürk Sanatoryum Training and Research Hospital Ethics Committee (Date:14.12.2022, Decision No: 2596). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

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Received: 20.12.2022 **Accepted:** 08.02.2023

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PCR (+) patients hospitalized between 01.05.2021 and 01.08.2022 in the 3rd level COVID Intensive Care Unit in the hospital were retrospectively examined.

The age, gender, BMI, co-morbidities of the patients, and which central venous route is preferred for the catheter will be determined. In addition, the number of punctures, thrombocyte count as well as the use of anticoagulants and acetylsalicylic acid, whether or not he/she received total parenteral nutrition (TPN), and how many days the catheter was left will be recorded and thrombotic events will be determined. Thrombotic events that developed in the patients were diagnosed by the radiologist with venous Doppler ultrasonography. All patients were given anticoagulants at the treatment dose (by adjusting the Low Molecular Weight Heparin treatment dose according to kg status). Since all patients are PCR (+) and are being treated with a diagnosis of COVID pneumonia, the treatment protocol is similar in all patients. All patients were followed up until discharge from the intensive care unit or mortality. When the patients were discharged from the intensive care unit, the catheters were removed because there was no need for a catheter.

RESULTS

The patients were grouped according to the central catheter location and the evaluations were made accordingly. When the difference between the groups was evaluated, a statistically significant difference was found in terms of gender, BMI, COPD and catheter day.

The rate of COPD co-morbidity in the subclavian catheterized group was statistically significantly higher than in the femoral and jugular catheterized group. However, we believe that this is a coincidence, even though it is statistically significant. COPD comorbidity is high because the hospital is a branch hospital of Chest Diseases.

The catheter day in the group with femoral catheters was statistically significantly lower than the group with jugular and subclavian catheters. We think that the catheter could not be used for a long time due to the complications and infection that developed.

Between 01.05.2021 and 01.08.2022, 110 patients who were followed up in the COVID intensive care unit and had a central venous catheter were examined. Of these patients, 64 had a femoral catheter, 32 had a jugular central catheter, and 14 had a subclavian catheter. The mean age of patients with femoral catheters was 69.45±14.09, those with jugular catheters were 70.25±10.03 years, and the mean age of patients with subclavian catheters was 70.21±16.84 years. The gender distribution of 110 patients was 56 males and 54 females. The gender distribution in the patient group with femoral catheters was 38 males and 26 females. In the patient group with jugular catheters, there are 16 males and 16 females. In the subclavian catheter group, there were 2 males and 12 females. The number of female patients in the subclavian catheterized group was statistically significantly higher than in the femoral and jugular catheterized group. However, although it is statistically significant, we believe that this result is coincidental.

While there was no significant difference between the groups in terms of age, a difference was found in the subclavian group in terms of female gender. The BMI of the patient group who underwent subclavian catheter was statistically significantly higher than the group who underwent femoral catheter.

The presence of diabetes mellitus, hypertension, chronic obstructive pulmonary disease (COPD), coronary artery disease (CAD) and malignancy were evaluated as co-morbidities of the patients. The COPD co-morbidity rate in the subclavian catheter-applied group is statistically significantly higher than in the femoral and jugular catheter-applied group. However, we believe that this is a coincidence, even though it is statistically significant. COPD comorbidity is high because the hospital is a branch hospital of Chest Diseases.

When evaluated in terms of coagulation parameters, prothrombin time (PT), international normalization ratio (INR), thrombocyte (plt) values of the patients were examined. No statistically significant difference was found between the groups.

Femoral catheter-related thrombosis was detected in 14 (21.9%) of 64 patients in the femoral catheter group. There were no complications in the jugular group. In the subclavian group, catheter-related thrombosis was observed in 1 patient. Thrombotic events that developed in the patients were diagnosed by the radiologist with venous Doppler ultrasonography.

There was no difference among the groups between the use of acetylsalicylic acid, the use of new generation oral anticoagulants and the use of low molecular weight heparin. There were no bleeding complications in any group.

The average Apache II score of the patients was 17 in the femoral group, 22 in the jugular group and 16.5 in the subclavian group, and no significant difference was found. In terms of Sequential Organ Failure Assessment Score (SOFA) averages, 10 were found in the femoral group, 11 in the jugular group, and 8 in the subclavian group. There was no statistically significant difference.

In terms of the duration of catheter use, the femoral group was used significantly shorter than the other groups. However, the rate of catheter-related thrombosis was found to be higher than the literature (**Table 1**).

Table 1: Variables according to central catheter location

	Central Catheter						p
	Femoral (n:64)		Juguler (n:32)		Subklavyen (n:14)		
	n	%	n	%	n	%	
Age, Year, $\bar{x}$±SD	69.45±14.09		70.25±10.03		70.21±16.84		0.955
Gender							0.009 [b,c]
Male	38	(59.4%)	16	(50.0%)	2	(14.3%)	
Female	26	(40.6%)	16	(50.0%)	12	(85.7%)	
BMI, $\bar{x}$±SD	27.09±3.20		27.68±3.47		29.68±3.46		0.033 [b]
TPN support							0.999
No	46	(71.9%)	23	(71.9%)	10	(71.4%)	
Yes	18	(28.1%)	9	(28.1%)	4	(28.6%)	
The use of oral anticoagulants							0.398
No	62	(96.9%)	29	(90.6%)	14	(100.0%)	
Yes	2	(3.1%)	3	(9.4%)	-		
The use of acetyl salicylic acid							0.326
No	55	(85.9%)	25	(78.1%)	10	(71.4%)	
Yes	9	(14.1%)	7	(21.9%)	4	(28.6%)	
Coronary artery disease							0.243
No	59	(92.2%)	26	(81.3%)	12	(85.7%)	
Yes	5	(7.8%)	6	(18.8%)	2	(14.3%)	
Cerebro vascular disease							0.527
No	57	(89.1%)	29	(90.6%)	11	(78.6%)	
Yes	7	(10.9%)	3	(9.4%)	3	(21.4%)	
Chronic obstructive pulmonary disease							0.021 [b,c]
No	50	(78.1%)	26	(81.3%)	6	(42.9%)	
Yes	14	(21.9%)	6	(18.8%)	8	(57.1%)	
Malignite							0.795
No	51	(79.7%)	25	(78.1%)	10	(71.4%)	
Yes	13	(20.3%)	7	(21.9%)	4	(28.6%)	
Diyabetes mellitus							0.148
No	39	(60.9%)	21	(65.6%)	5	(35.7%)	
Yes	25	(39.1%)	11	(34.4%)	9	(64.3%)	
Hypertension							0.512
No	30	(46.9%)	19	(59.4%)	7	(50.0%)	
Yes	34	(53.1%)	13	(40.6%)	7	(50.0%)	
Heart failure							0.700
No	54	(84.4%)	28	(87.5%)	11	(78.6%)	
Yes	10	(15.6%)	4	(12.5%)	3	(21.4%)	
Number of punctures							0.652
1	59	(92.2%)	28	(87.5%)	12	(85.7%)	
2	4	(6.3%)	3	(9.4%)	2	(14.3%)	
3	1	(1.6%)	1	(3.1%)	-		
Complication							0.308
No	50	(78.1%)	29	(90.6%)	11	(78.6%)	
Yes	14	(21.9%)	3	(9.4%)	3	(21.4%)	
Types of complications							0.999
Femoral tromboz	14	(100%)	3	(100%)	2	(66.7%)	
Subklavyen tromboz	-		-		1	(33.3%)	
Catheter day, med (IQR)	8 (4)		13 (7)		21 (7)		<0.001 [a,b]
Apache, med (IQR)	17 (7.5)		22 (13.5)		16.5 (13)		0.072
Sofa, med (IQR)	10 (8)		11 (9)		8 (10)		0.243
Platelet count, Med (IQR)	175 (45)		189.5 (36)		194.5 (33)		0.191

Continuous variables are expressed as either the mean ± standard deviation (SD) or as the median (IQR) and categorical variables are expressed as either frequency (percentage). Continuous variables were compared with one way anova or test by kruskal wallis test and categorical variables were compared using Pearson's chi-square test or fisher exact test. Statistically significant p-values are in bold. LSD test was performed for the binary comparisons among the groups and the p value was set at 0.05. Significant differences were found between; a: Femoral vs Juguler, b: Femoral vs Subklavyen, c: Juguler vs Subklavyen
BMI:Body mass Index TPN:Total parenteral nutrisyon

DISCUSSION

COVID-19 pneumonia is a disease that generally occurs with respiratory symptoms such as cough, fever, shortness of breath and weakness. In addition, it also causes vascular pathologies, including hypertension and an increase in thrombotic events in patients. In the autopsies of deaths caused by COVID, it has been shown that there is endothelial damage due to the virus that causes death in lung cells (2).

After the 1950s, central venous catheter applications started to increase gradually due to medical treatment applications and central venous pressure monitoring (5). Many complications related to the catheterization procedure have been described, and these are briefly hematoma formation, great vessel injury, pneumothorax, hemothorax, thrombosis, embolism, and catheter malposition. More than one factor has been held responsible for the development of thrombosis. Application of more than one catheter from the same area, the duration of the catheter and the position of the tip of the catheter are important factors for the development of thrombosis (5,6).

In COVID patients followed in the intensive care unit, there is a need for a central catheter in terms of continuous blood gas monitoring, other medical treatments and parenteral nutrition support due to oral intake insufficiency. In the studies carried out, it has been reported that procedures performed close to the patient's airway are a risk factor for transmission of COVID infection. The doctors who performed the procedure were infected despite wearing personal protective equipment (7). Intensive care physicians also preferred femoral catheters to protect themselves because the patient is further away from the airway (8). According to our clinical experience, since we think that the incidence of femoral catheter-related thrombosis is high, the frequency of internal jugular vein and subclavian catheter applications has been increased in SARS-CoV-2 patients in our clinic.

As mentioned in the literature, parenteral nutritional support is recommended for patients who cannot get enough calories, as the constant air hunger and hypoxia in COVID patients prevent patients from getting enough daily calories orally (8). Although it is found in the literature that TPN application is also effective in the development of thrombosis in the catheter and that the risk increases gradually with advanced age, TPN did not increase the risk of thrombosis in our study (9).

It may cause complications such as catheter-related thrombosis, pulmonary embolism, recurrent deep vein thrombosis, post-thrombotic syndrome and sepsis. These complications may be silent or cause severe symptoms (10). In the 1990s reported that up to 10% of patients with symptomatic catheter-related thrombosis could detect pulmonary embolism (11). However, a recently published study of 4000 patients with central venous catheters did not report any symptomatic pulmonary embolism complications (12).

Symptoms of thrombus and superior vena cava syndrome (edema in the arms, face and neck, enlargement of the chest veins, headache, cough, and dyspnea) may occur in patients undergoing central venous catheter application (13,14).

Due to the increasing number of central venous catheter applications, the rate of DVT seen in the upper and lower extremities has also increased. The incidence of thrombosis developing in the lower extremity due to femoral catheter applications has been shown to be around 21%, the highest in the literature (15). Venous Doppler ultrasonography is preferred in the diagnosis of thrombosis with the presence of clinical symptoms, because it is easy to apply, low cost, does not require any intervention, has high specificity, and distinguishes the presence or absence of flow (16). In the study, the presence of thrombosis was detected by Doppler ultrasonography.

In our study, the incidence of thrombosis in the SARS-CoV-2 patient group with femoral catheter was 21.9% and it was found to be higher than the literature. Since we saw the incidence of thrombosis in the femoral central catheter as relatively high with our clinical experience, it was no longer our preference for the femoral vein-priority central catheter in COVID -19 patients.

Removal of the catheter is important for in the treatment of central catheter-related thrombosis.

Low molecular weight heparin (LMWH) is a major choice in the treatment of central catheter-related thrombosis too. In addition, vitamin K antagonists, unfractionated heparin and fibrinolytic agents can also be used (17). Management of central venous catheter-related thrombosis may also affect developing complications. In a study, 112 patients who developed catheter-related thrombosis did not improve their symptoms when treatment was continued only without anticoagulation and without removal of the catheter (18).

Prolonged use of the same port or catheter increases the risk of symptomatic catheter-related thrombosis will occur. Therefore, international guidelines recommend removing central venous catheters as soon as they are not needed (19).

In our clinic, prophylactic LMWH dose is routinely used in intensive care for non- COVID patients, and therapeutic LMWH dose is applied in SARS-CoV-2 patients. In our clinical observations, we believe that the frequency of thrombosis is higher in SARS-CoV-2 patients, but comparative studies are needed on this subject in the COVID - non-COVID patient group.

Among the factors of catheter-related thrombosis, construction materials also gain importance. It has been reported that polyvinylchloride, Teflon, poly-ethylene catheters are more thrombotic than polyurethane and silicone catheters, and silicone catheters are also reported to be less thrombotic than polyurethane catheters (20). Polyurethane catheter is used in our clinic, but it should not be forgotten that the risk of thrombus development will not completely disappear with any catheter production material.

CONCLUSION

SARS-CoV-2 is a thrombotic disease that affects all vascular structures and causes serious mortality and morbidity. Unnecessary procedures should be avoided as vascular interventions in these patients may cause serious complications in patients. In addition, we believe that choosing the subclavian or internal jugular vein instead of the femoral vein in the application of central venous catheter will reduce the development of thrombosis. In this regard, supportive, multicenter and comparative studies are needed.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ankara Atatürk Sanatoryum Training and Research Hospital Ethics Committee (Date:14.12.2022, Decision No: 2596)

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

REFERENCES

1. Berlin DA, Gulick RM, Martinez FJ. Ciężki COVID-19. N Engl J Med 2020; 383: 2451-60.
2. Kashi M, Jacquin A, Dakhil B, et al. Severe arterial thrombosis associated with COVID COVID-19 infection. Trombosis Research 2020; 192: 75-7.
3. Henry BM, Vikse J, Benoit S, Favaloro EJ, Lippi G. Hyperinflammation and derangement of renin-angiotensin-aldosterone system in COVID-19: a novel hypothesis for clinically suspected hypercoagulopathy and microvascular immunothrombosis. Clinica chimica acta 2020; 507: 167-73.
4. Spiezia L, Boscolo A, Poletto F, et al. COVID-19-related severe hypercoagulability in patients admitted to intensive care unit for acute respiratory failure. Thromb Haemost 2020; 120: 998-1000.
5. Forauer AR, Theoharis CG, Dasika NL. Jugular vein catheter placement: histologic features and development of catheter-related (fibrin) sheaths in a swine model. Radiology 2006; 240: 427-34.
6. Liangos O, Gul A, Madias NE, Jaber BL. Long-term management of the tunneled venous catheter. Semin Dial 2006; 19: 158-64.
7. Tayebi P. Jugular vein catheterization in critically ill patients with corona virus disease 2019 can increase the surgeon's exposure. Vasc Specialist Int. 2020; 36: 201–2.
8. Scoppettuolo G, Biasucci DG, Pittiruti M. Vascular access in COVID-19 patients: Smart decisions for maximal safety. The Journal of Vascular Access. 2020; 21: 408-10.
9. Geerts W. Central venous catheter-related thrombosis. Hematology Am Soc Hematol Educ Program. 2014; 1: 306-11.
10. Monreal M, Raventos A, Lerma R, et. al. Pulmonary embolism in patients with upper extremity DVT associated to venous central lines—a prospective study. Thromb Haemost 1994; 72: 548-550.
11. Chopra V, Anand S, Hickner A, et. al. Risk of venous thromboembolism associated with peripherally inserted central catheters: a systematic review and meta-analysis. Lancet 2013; 382: 311-25.
12. Grant JD, Stevens SM, Woller SC, et. al. Diagnosis and management of upper extremity deep-vein thrombosis in adults. Thromb. Haemost 2012; 108: 1097-108.
13. Akoğlu H, Yılmaz R, Peynircioğlu B, et al. A rare complication of hemodialysis catheters: Superior vena cava syndrome. Hemodialysis Inter 2007;1 1: 385-91.
14. Gray BH, Olin JW, Graor RA, Young JR, Brtholomew JR, Ruschhaupt WF. Safety and efficacy of thrombolytic therapy for superior vena cava syndrome. Chest 1991; 99: 54-9.
15. Romano L, Bilotta F, Dauri M, et al. Short Report- Medical nutrition therapy for critically ill patients with COVID -19. Eur Rev Med Pharmacol Sci. 2020; 24: 4035-9
16. Rooden CJ, Tesselaar ME, Osanto S, Rosendaal FR, Huisman MV. Deep vein thrombosis associated with central venous catheters- a review. J Thromb Haemost. 2005; 3: 2409-19.
17. Kreuziger LB, Jaffray J, Carrier M. Epidemiology, diagnosis, prevention and treatment of catheter-related thrombosis in children and adults. Thromb Research 2017; 157: 64-71.
18. Frank D.A., Meuse J., Hirsch D., Ibrahim J.G., Van den Abbeele A.D.: The treatment and outcome of cancer patients with thromboses on central venous catheters. J. Thromb. Thrombolysis 2000; 10: 271-5.
19. Farge D, Bounameaux H, Brenner B, et al. International clinical practice guidelines including guidance for direct oral anticoagulants in the treatment and prophylaxis of venous thromboembolism in patients with cancer. Lancet Oncol 2016; 17: e452-e466.
20. Yosunkaya A, Çelik JB, Dayıoğlu M, Erkoçak R, Paksoy Y. Santral ven kateterizasyonuna bağlı tromboz ve superior vena kava sendromu. Türk Anest Rean Der Derg 2009; 37: 108-13.